Section of Otology

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The Pathology, Symptomatology and Diagnosis of Certain Common Disorders of the Vestibular System

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INTRODUCTION

IT is generally agreed that within the last fifteen years some extension has been achieved of our understanding of the problems of human vertigo. Nevertheless, difficulties and confusion still persist and in the course of the present communication an attempt will be made to advance the process of its clarification, both by critical review and by a short account of some of our recent investigations. The foundations of the subject are to be found in the writings of Prosper Ménière, and these we take as our starting point.

Ménière's papers on vertigo are chiefly remarkable for the powers which their writer displays of describing and analysing the symptoms and signs of disease. It is easy now to realize that it was this mastery of symptomatology which, more than anything else, enabled him to identify, with an accuracy which has never been seriously questioned, the disease of the labyrinth which has since come to bear his name. Beyond, however, asserting with confidence that the disease was due to a lesion of the internal ear, limited to that organ and indestructive to life, he made no *direct* observations upon its pathological anatomy, and further information upon this point was not forthcoming until 1938. Since then the morbid anatomical basis of the disease has been established by means of histological examinations of the temporal bones in a number of clinically characteristic cases. It is fair to say that this opinion is not perhaps a universal one. On the contrary, it is still sometimes said that Ménière *did* describe the pathological anatomy of Ménière's disease, and reference is made to the case which Ménière cited of the young girl who died after a short illness, due to a chill, in the course of which she suffered from deafness, vertigo and vomiting. Ménière examined the temporal bones and found a reddish exudate in the semicircular canals. But no reader of his text could suppose that Ménière wished it to be inferred from this observation that the cause of *this* girl's illness was the same as that responsible for the recurrent attacks of vertigo with deafness so characteristic of the other, but essentially benign, disease which he had described so clearly. Indeed, the fatal issue of the case alone rules out this possibility.

Our own view is that Ménière's reference to the anatomical changes in these labyrinths had an entirely different significance and one, moreover, which is quite obvious from the context.

It is necessary to bear in mind that in 1861, when Ménière published his best-known paper, the very possibility that a lesion of the internal ear could cause such severe symptoms as vertigo and vomiting was still a moot point.

Flourens' experimental work on pigeons, in which he demonstrated for the first time that gross disorders of equilibrium could be produced by injury of the semicircular canals, had only been published some thirty years earlier, and its significance as regards the problems of human disease had not yet been appreciated. It was Ménière's great merit that he knew of Flourens' work and understood its meaning. To him, therefore, the significance of the exudate in the semicircular canals of his patient was that in it he recognized the vital link so far missing between Flourens' animal experiments and the problem of human vertigo, a demonstrable lesion of the semicircular canals in a subject who had suffered in life from vertigo. Ménière argued that if such a hæmorrhagic lesion, occurring in the course of this girl's fatal illness, could produce vertigo, then other lesions of the inner ear, be their precise nature what you will, could also be the cause of the vertigo in his other group of subjects whose symptoms he had described with such care. There Ménière left the matter. He had identified his disease by his accurate specification of its symptomatology and natural history. As to its pathology he said only this: " La lésion matérielle réside dans les canaux semicirculaires"—"the essential lesion is situated in the semicircular canals". Little more knowledge came our way until 1938 when Cairns and Hallpike examined the temporal bones of their two subjects and established the nature of Ménière's lesion [1].

Of this the essential abnormality was a distension without evidence of infection or trauma of the endolymphatic vesicle; a finding, remarkable in itself and since reproduced with remarkable uniformity in a considerable number of further histological studies of the temporal bones carried out by Hallpike and also by a number of others.

To summarize this chapter of history it can be said that Ménière's concept was of a disease *sui generis* of the internal ear. This he based in the main upon his own studies of symptomatology and supported it by

certain *in*direct evidence of animal expermentiation and of human pathology. Since 1938 this concept has been abundantly confirmed by further clinical studies and by *direct* pathological evidence derived from the study of human temporal bones.

This analysis of Ménière's work and the position it occupies in the much larger field of organic vertigo as we know it today was clearly stated by Cairns and Hallpike in their original paper, and has since gained wide acceptance by a number of American authors, in particular Day [2], Wells [3] and Williams [4]. But since Ménière's time this field has become much enlarged and its contours very confused and it has been customary to mix together with Ménière's disease, under the undiscriminating label of Ménière's syndrome or even of pseudo-Ménière's disease, other types of organic vertigo which conform only vaguely to the established symptomatology and pathology of Ménière's disease. In the past this has been unavoidable, and connotes only our ignorance of the clinical and pathological features of these disorders which would enable us to distinguish them from each other and from Ménière's disease.

It is, of course, the task of oto-neurological research to resolve this ignorance. When complete, it will be possible so to distinguish them and call them by names which will announce their clinical and pathological individualities. When that time comes the need for the label, Ménière's syndrome, will disappear and no more will be heard of that lexicographical abomination, "pseudo-Ménière's disease". The task has been begun with the clinico-pathological work carried out during the last fifteen years upon Ménière's disease. During this, we have seen rescued from the confusion what Ménière put into it—his disease—with its symptomatology confirmed and its pathology established. It is the purpose of the present communication to present certain new information upon the subject of Ménière's disease. In addition, descriptions will be given of two other varieties of organic vertigo; one a disorder of the vestibular neurones; another a disorder of the otolith system in the labyrinth. Both of these are liable to be confused with Ménière's disease, and carry Ménière's name on that familiar label "Ménière's Syndrome". It will, however, be shown that their clinical and pathological features make obvious their distinction from Ménière's disease, and other labels will accordingly be proposed for them which declare this distinction and are more appropriate to their symptoms, signs and pathological anatomy.

In the present work we have endeavoured first and foremost to make use of the clinical methods in which Ménière himself so excelled. That is to say, it has been our aim to base our opinions primarily upon the study of symptoms and natural history of disease. To this we have added as much evidence as possible from the physical signs which can now be derived from modern tests of cochlear and vestibular function. Finally, when the opportunity has presented itself we have been able to check our clinical evidence by histological studies of the temporal bones.

Part I.—Ménière's Disease

On symptomatology there is little to add to Ménière's original description and to the analysis published in 1942 by Cawthorne *et al.* [5]. We make more, perhaps, of distortion of hearing than Ménière did, and of the exacerbation of tinnitus and deafness during the attacks. But these can hardly be described as major developments. As regards physical signs we find the vestibular test results are still very much as previously stated [5]. In particular the caloric test results are abnormal in 94% of cases. Of these, 20% show a directional preponderance towards the sound ear. In 58% there is a loss of canal sensitivity in the affected ear. In 16% the result represents a mixture of these two primary derangements. In the field of tests of cochlear function, however, we are able to report considerable progress since 1942. Dix *et al.* [6] showed in 1948 that the phenomenon of loudness recruitment was invariably present in Ménière's disease, and that in a proportion of such subjects over-recruitment made its appearance. In another series of observations Hood [7] has been able to show that the phenomenon of adaptation is abnormally rapid in cases of Ménière's disease. Speech audiometry, too, has in many cases given results in cases of Ménière's disease which have a high diagnostic significance. In particular they reveal a loss of intelligibility which is out of proportion to the pure tone audiometric threshold loss. It will be recalled that in the publication to which reference is made [6], the characteristically positive finding of recruitment in Ménière's disease was compared with its characteristic absence in cases of VIII nerve tumour, and thereon was based our opinion that the phenomenon of recruitment was attributable to hair-cell disease. For this argument pathological evidence is in some cases very strong. That is to say, the cells of Corti's organ show very striking changes while the cochlear nerve fibres and the cells of the spiral ganglion are quite normal. This is exemplified in the following photomicrographs of the organ of Corti in the normal and affected ears in the first of the two cases of Ménière's disease described (Figs. 1 and 2). [1]. (For Figs. 1 to 6 *see* pp. 347 and 348.)

In other cases, however, examined both by ourselves and others, these changes in the hair cells are by no means obvious, and to circumvent the difficulty it has been necessary to have recourse to the argument that in such cases the histological changes responsible for the deafness and recruitment were of a kind which made it possible for them to be masked by the considerable histologic artefacts which are so often unavoidable with human material. If this argument be accepted, then with it must also be accepted the likelihood that in a case of unilateral Ménière's disease, in which this histological artefact was reduced by exceptionally favourable conditions of fixation, it should be possible to distinguish some significant anatomical changes in the hair cells. A brief account of clinical and pathological data derived from such a case now follows:

The case was that of a man of 54 who died in 1949. In 1938 he began to suffer from attacks of paroxysmal vertigo, during which objects rotated vertically. They were accompanied by nausea and

lasted from ten to thirty minutes. Consciousness was not lost during the attacks, during which he was compelled to lie down. He had experienced such attacks yearly until 1945. During that time he also had buzzing tinnitus in the right ear and deafness which was progressive. He was seen at Sir Charles Symonds' Out-Patients in November 1948 on account of epileptic attacks lasting for half an hour or more, during which he became unconscious. Soon after, he developed drowsiness, confusion and a severe affection of speech. He was admitted to Queen Square on February 9, 1949, where a diagnosis was made of a left temporal lobe neoplasm. This was confirmed by biopsy; the patient died six days later. At post-mortem a large tumour was found in the left temporal lobe which histological examination showed to be an astrocytoma. Apart from some herniation of the inner edge of the left temporal lobe through the incisura tentorii on the left-hand side and some cerebellar coning, there was no other abnormality of the cerebrum, cerebellum, brain-stem, cranial nerves or meninges. The last otological examination was carried out at Guy's in December 1948 when the findings confirmed the diagnosis of Ménière's disease, the nose and throat being found healthy, the tympanic membranes normal with a severe degree of deafness of the right ear of the perceptive type. Pure tone audiometry showed an approximately uniform hearing loss on the right side of some 60 to 70 decibels. There was, in addition, a slight high-tone loss in the left ear confined to the frequencies 4,000 and 8,000 cycles. Caloric responses showed a slight reduction of the responses to both cold and hot stimuli on the right-hand side. We were able to obtain the temporal bones sixteen hours after death, and to undertake their fixation and preparation ourselves. It was possible to display the histology of the labyrinths in a comparatively good state of preservation; in particular, the condition of the hair cells was sufficiently free from post-mortem artefact to make worth while a close morphological comparison of Corti's organ in the two ears.

In Fig. 3 is shown the unaffected cochlea with a normal spiral ganglion and a well-preserved organ of Corti with Reissner's membrane in its normal position.

In Fig. 4 is shown the affected cochlea; the spiral ganglion is of normal density. The general structure of Corti's organ can be made out, although not in any great detail. Finally, the typical distension of the scala media is seen with the displacement of Reissner's membrane.

To facilitate comparison of the structure of Corti's organ in these two labyrinths, photomicrographs have been prepared in which views of the organ in the different coils of the unaffected cochlea are presented at high magnification side by side with their counterparts in the affected cochlea.

In Fig. 5 are shown the organs of Corti in the anterior and posterior middle coils. The organs of the right or affected cochlea are on the right-hand side. On the left, the normal side, the normal form and size of Corti's organ is well preserved in both coils. Both rods of Corti are well seen, and the form of Corti's tunnel is nearly normal. In both coils can be seen what is probably the remains of a hair cell and its nucleus. On the affected side obvious changes are present. Thus, the total size of Corti's organ is reduced, its shape is irregular, the outer rod has been demolished and the hair cell framework has disappeared. In addition, Corti's tunnel, or what is left of it, seems to be occupied by a kind of coagulum.

In Fig. 6 are shown the anterior and posterior basal coils. As before, the right or affected organ of Corti is shown on the right. On the left or normal side, Corti's tunnel is preserved and the organ is of normal size and shape. There is distinct evidence of at least one hair cell nucleus, while a nerve filament is to be seen crossing Corti's tunnel. On the affected side, however, the outer rod of Corti has disappeared and some coagulum is present in the space of what was Corti's tunnel. Finally, the area occupied by the hair cells seems to be disorganized, both as regards its shape and its cellular contents.

These changes have been demonstrated in some detail since they strengthen in a very satisfactory manner, what has been a weak link in the chain of argument, which has led us to conclude that the deafness in Ménière's disease and the loudness recruitment phenomenon which is so characteristic of it are attributable to hair-cell disease.

PART II.—VESTIBULAR NEURONITIS

We come next to another group of patients whose chief symptom is again vertigo, usually but not always paroxysmal in character. This group is chiefly distinguished from Ménière's disease on clinical grounds by the conspicuous absence of cochlear signs and symptoms. We began to recognize this condition at our Clinic at Queen Square as a distinct clinical entity in about 1946. For a variety of reasons, to which further reference will be made, it seemed then attributable, beyond any doubt, to some form of organic disease confined to the vestibular apparatus and localized, in all probability, to its peripheral nervous pathways up to and including the vestibular nuclei in the brain-stem. It was impossible, however, to go further and specify the particular elements of the neurones, cells or fibres, which were affected. When, therefore, it came to naming the condition we required a term comprehensive enough to encompass this uncertainty. We chose the name "vestibular neuronitis" and have since continued to use it.

We first described the condition in 1949 in a short communication to the Fourth International Congress of Oto-laryngology in London [8] and our present analysis of its clinical features is based

upon the study, made possible through the courtesy of our colleagues at Queen Square, of over 100 cases. These we have examined in the course of the last few years. Age and sex distribution are tabulated as follows:

TABLE I

Age	*Age Distribution*							*Sex Distribution*			
(years)	Under 20	20–29	30–39	40–49	50–59	Over 60	Total	Male	57		
Number ..	5	21	37	22	14	1	100	Female	43	Total	100

It will be seen that the disorder chiefly affects the age group 30 to 50 without preference for sex. Apart from the absence of cochlear signs and symptoms the condition is often but not always distinguishable from Ménière's disease by the character of the vertigo. This may consist of sudden and transient seizures accompanied by sensations of blackout. On the other hand there may be no severe paroxysms and the disequilibrium may take the form of "feeling top heavy" or "off-balance", particularly when walking or standing. As in other forms of organic vestibular disease, the disequilibrium is aggravated by head movements of all kinds. In a fairly high proportion of the subjects the onset of the symptoms is associated with some kind of febrile illness, or with evidence of infection of the ears, nose and throat, and to this aspect of the malady we shall later return.

Otoscopic findings are typically normal with normal test results of cochlear function including pure tone audiometry.

When we come to investigate vestibular function, however, very marked abnormalities are always present, in particular of the caloric responses which are consistently reduced, often grossly so, and on both sides. A full description of the caloric abnormalities follows: All tests were carried out in accordance with the technique described by Fitzgerald and Hallpike [9]. We have divided our test results in accordance with the following nomenclature:

(1) *Complete canal paresis.*—No response obtained with irrigation at 20° C. for one minute.

(2) *Severe canal paresis.*—No response obtained with stimuli of normal strength, i.e. 30° C. or 44° C. for 40 seconds; a response, however, was obtained with water at 20° C. for one minute.

(3) *Moderate canal paresis.*—In this group responses, although obviously reduced, were obtained with stimuli of normal strength.

Certain of the cases exhibited directional preponderance, and others a combination of directional preponderance and canal paresis. For further particulars of the qualitative and quantitative assessment of abnormalities of the patterns of the caloric test results reference should be made to previous publications [5, 10].

The abnormalities were further divided into two main groups:

(1) Bilateral. (2) Unilateral.

The complete classification is given in Table II.

TABLE II.—CALORIC ABNORMALITIES

Bilateral:	Complete canal paresis ..	7	*Unilateral:*	Complete canal paresis ..	8
	Severe canal paresis ..	25		Severe canal paresis ..	9
	Moderate canal paresis ..	7		Moderate canal paresis ..	20
	Combined canal paresis with directional preponderance to the same side	8		Combined canal paresis with directional preponderance to the opposite side	8
	Total	47		Directional preponderance to the opposite side ..	8
				Total	53

It will be seen from Table II that substantial abnormalities of the caloric responses were present in all of our 100 cases. In 47 they were bilateral; in 53 they were unilateral.

In a few of the cases the abnormalities of the caloric test findings have been shown by follow-up to be the first and only manifestation of disseminated sclerosis. In the great majority, however, there was no evidence whatsoever of extra-vestibular nervous disease, and in these we have postulated an organic lesion of the vestibular nervous pathways at some point up to and including the vestibular nuclei, a vestibular neuronitis. We have preferred to believe that the lesion is central to the labyrinth in accordance with a well-established principle of oto-neurology, namely that destructive labyrinthine lesions, whatever their pathology, tend on the whole to involve the cochlear apparatus. Furthermore, a high proportion of our subjects have been found to exhibit significant changes of the galvanic test responses, evidence which is strongly indicative of a lesion central to Scarpa's ganglion. Later reference will be made to the technique and interpretation of these tests.

The condition is essentially a benign one. It responds well to treatment of focal infection when this is present, and generally recovers in the course of a few years. In a few cases we have observed the re-establishment of the caloric responses.

We propose now to consider in greater detail two important clinical aspects of the condition:

(1) The role of infection as a pathogenic factor.

(2) The galvanic test results and their localizing value.

(1) *The role of infection as a pathogenic factor.*—The role of focal infection as a cause of organic vertigo has been discussed by a number of authors, notably by A. J. Wright [11] and particular attention was directed to this point by Cawthorne *et al.* [5]. The evidence adduced therein showed that in subjects in whom the diagnosis of Ménière's disease had been made upon the basis of an adequate analysis of symptomatology and physical signs, infective foci in the nose and throat occurred so rarely as to make it difficult to attach thereto any causal significance. In vestibular neuronitis, however, our clinical investigations have led us to the conclusion that infective foci in the nose and throat play an important part in its pathogenesis. This view is based chiefly upon a study of 50 of our cases in whom, in addition to a routine examination of the nose and throat, we have also carried out blood examinations including sedimentation rates and radiological examination of the paranasal sinuses. The sedimentation rate tests were carried out according to the Westergren technique. We have regarded as pathological values for the first hour which exceed 8 mm. in the male or 10 mm. in the female.

Our 50 cases fall into the following three main divisions with certain subgroups:

DIVISION I.—CASES PRESENTING DIRECT EVIDENCE OF AN ACTIVE INFECTIVE FOCUS.

Group A. Antral infection confirmed by the presence of pus on proof puncture: Number of cases, 10. In 4 of these the sedimentation rate was raised.

Group B. Sore throats with obvious evidence of active tonsillar infection: Number of cases, 2. In both, the sedimentation rate was raised.

DIVISION II.—CASES PRESENTING STRONG PRESUMPTIVE EVIDENCE OF AN ACTIVE OR QUIESCENT INFECTIVE FOCUS.

Group A. Definite radiological evidence of antral infection: Number of cases, 6. In some, proof puncture was refused; in others it was negative. In none of these was the E.S.R. raised.

Group B. Dental infection: Number of cases, 4. The E.S.R. was raised in one case.

Group C. Cases presenting no evidence of infective focus, but giving a clear history of an infective illness at the time of onset of the vertigo: Number of cases 13. In 3 of these the sedimentation rate was raised.

DIVISION III.—CASES PRESENTING NO EVIDENCE OF AN INFECTIVE FOCUS, OR A HISTORY OF INFECTIVE ILLNESS.

Number of cases, 15. In 4 of these the sedimentation rate was raised.

Our opinion, based upon these findings, that infective processes play an important part in the pathogenesis of vestibular neuronitis, is chiefly derived from the two groups of cases comprised in Division I. From these we see that clear evidence of antral or tonsillar infection was present in 24% of our 50 cases. This far exceeds any corresponding figures that we could base upon our experience of Ménière's disease. The same can be said of Division II, from which we see that 46% of our 50 cases either gave a clear history of an infective illness at the time of onset of the vertigo, or else exhibited significant evidence of an infective focus in the nose and throat.

In the other 50 of our 100 cases our examinations for evidence of focal infection have been less complete; that is to say, systematic sinus X-rays and blood examinations have not been carried out. Nevertheless, in these remaining 50 cases we have observed clear evidence of antral infection in 8, and in 14 others there was history of an infective illness at the time of the onset of the symptoms.

(2) *The galvanic test results and their localizing value.*—The use of the galvanic tests in vestibular neuronitis would appear to be particularly appropriate since the work of Huizinga [12], Dohlman [13] and others has suggested that the galvanic responses depend upon the integrity of Scarpa's ganglion and the vestibular neurones central thereto, and are preserved in lesions of the peripheral sense organs. We have, therefore, carried out systematic galvanic tests in a number of our patients [14]. Details of the test procedure are given as follows:

"Bipolar stimulation was used, the current being passed between brine-soaked pads firmly located upon one or other of the mastoid processes and the manubrium sterni. The tests were carried out with the patient standing with eyes closed and the feet and heels close together. The reaction was described as positive when swaying, which normally occurs towards the ear carrying the positive electrode (anode), could be clearly and repeatedly observed. Corresponding observations were also carried out with the polarity reversed; in these circumstances, of course, the direction of the swaying was also reversed. . . .

"To begin with, a series of control observations was carried out upon 12 normal individuals with no history of ear disease or vertigo. In all of these it was found possible to observe positive responses with values of current lying within the range of 0·3 to 1·9 mA., with an average value of 0·8 mA."

Full details of these findings are given in Table III, while the values obtained in 16 cases of vestibular neuronitis are given in Table IV. In both tables the figures given are for milliamperes of current at threshold. The maximum currents given in Table IV were determined by the onset of the usual painful sensations from the skin areas underlying the electrodes.

TABLE III.—12 NORMAL SUBJECTS

Ear Stimulated

	Right		Left	
	Polarity		Polarity	
Case No.	−ve	+ve	−ve	+ve
1	0·6	0·3	0·6	0·6
2	0·5	0·45	0·5	0·45
3	0·5	0·5	0·4	0·6
4	0·5	0·7	0·5	0·7
5	1·0	1·0	0·5	1·2
6	0·45	0·4	0·45	0·4
7	1·4	1·5	1·4	1·5
8	1·0	1·3	1·0	1·4
9	0·5	0·7	0·5	0·7
10	0·45	0·4	0·45	0·4
11	0·6	0·6	0·55	0·55
12	1·8	1·9	1·7	1·8

(Table III is quoted from *Brain*, 1949, **72**, 243.)

TABLE IV.—16 CASES OF VESTIBULAR NEURONITIS

Ear Stimulated

	Right			Left		
Case No.	Polarity		Max. current used	Polarity		Max. current used
	−ve	+ve		−ve	+ve	
1	Absent	3·0	4·0	1·3	1·2	
2	Absent	Absent	5·0	Absent	Absent	5·0
3	1·4	1·4		0·6	0·6	
4	0·7	0·7		3·0	3·0	
5	1·6	1·6		1·4	1·4	
6	2·0	3·0		3·0	3·0	
7	Absent	Absent	3·0	Absent	Absent	3·0
8	1·2	1·5		1·2	1·5	
9	1·0	3·0		4·0	1·0	
10	Absent	Absent	5·0	Absent	Absent	5·0
11	Absent	1·5	3·0	1·5	Absent	3·0
12	0·5	1·0		0·7	0·6	
13	Absent	Absent	2·2	Absent	Absent	2·2
14	1·0	4·0		5·0	5·0	
15	Absent	Absent	5·0	Absent	Absent	5·0
16	0·6	0·6		1·0	1·0	

It will be seen that in all, except 3 cases, a significant reduction of the galvanic responses was present, a finding which is certainly suggestive of a lesion of the vestibular neurones involving either Scarpa's ganglion, or the vestibular neurones central thereto. It must be added, however, that the mechanism of the galvanic responses is in some ways obscure, and we have observed their derangement both in cases of severe and long-standing Ménière's disease and in certain other disorders in which it might be supposed that the vestibular end organs are chiefly or solely involved. This finding would be explained upon the reasonable supposition that the response to galvanic stimulation is mediated, at least in part, by the peripheral sense organs. If these are eliminated by disease, then the responses will be reduced but not abolished. The matter is further complicated by the fact that long-continued and heavy sedation is likely in cases of Ménière's disease to reduce the sensitivity of the central vestibular elements. For this reason, too, one would expect, in long-standing cases of Ménière's disease, to encounter some reduction of the galvanic responses. The subject, however, is a difficult one and clearly calls for further examination. So far, however, as we have considered the matter, it would seem clear that the reduction of the galvanic responses in vestibular neuronitis exceeds in degree what we have encountered in Ménière's disease, and therefore supports our hypothesis of a central affection of the vestibular neurones.

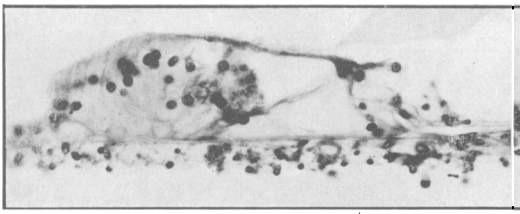

FIG. 1.—Organ of Corti. Normal cochlea. The organ is of normal form and size, with good preservation of Corti's tunnel. Details of the hair cells are obscured by post-mortem degeneration. (× 194.)

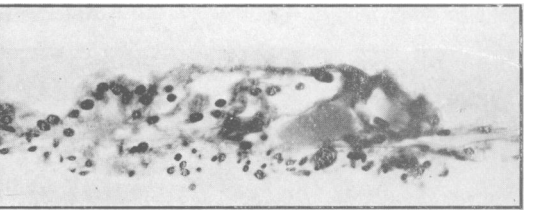

FIG. 2.—Organ of Corti. Affected cochlea. The organ is shrunken and its outline irregular. Corti's tunnel is occupied by a structureless coagulum. (× 194.)

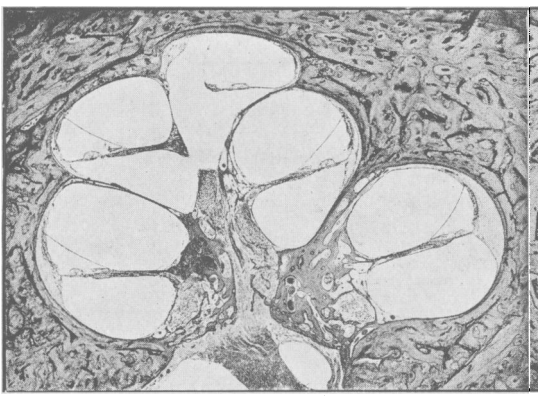

FIG. 3.—(× 10.)

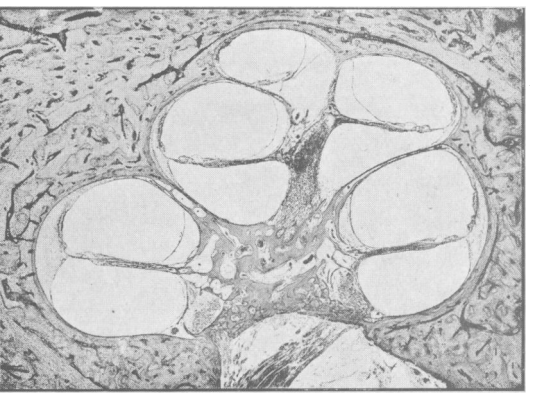

FIG. 4.—(× 10.)

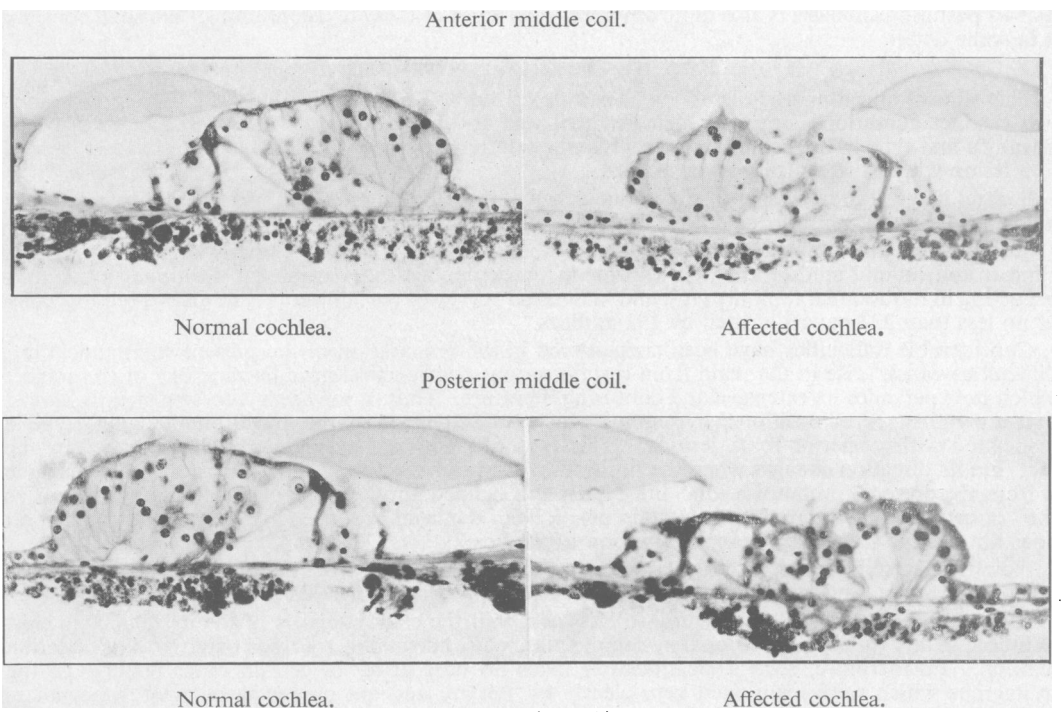

FIG. 5.—(× 194.)

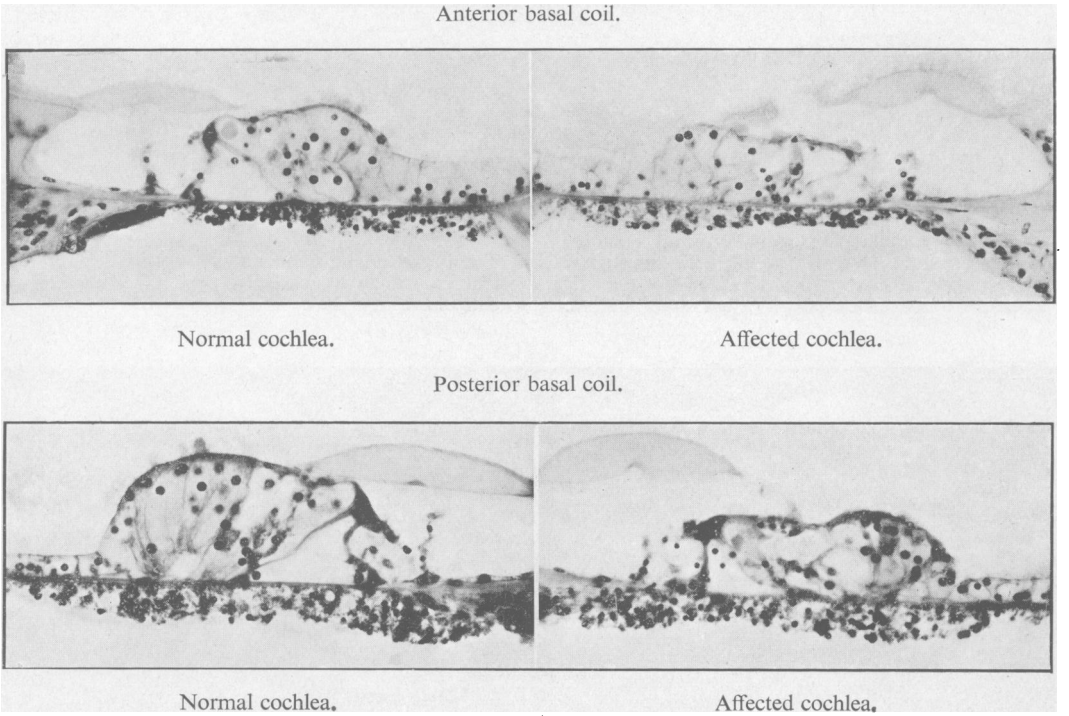

FIG. 6.—(× 194.)

We come, finally, to a third variety of organic vertigo presenting as its chief clinical feature a highly distinctive type of positional nystagmus. This again is distinguishable on clinical grounds alike from Ménière's disease and from vestibular neuronitis. Further, we have good reason to believe that its pathological basis is also quite different from those of these two conditions. We shall consider it in some detail.

PART III.—POSITIONAL NYSTAGMUS

This strange and dramatic disorder was first described by R. Bárány in 1921 [15]. Bárány mentions two distinct conditions, one of which he attributed to otolith disease. This we shall describe as Bárány's first type. His second type, to which he referred very cursorily, he seems to have attributed to a lesion within the central nervous system.

Bárány had not a great deal to say about either of these conditions, but what he did say was very much to the point, and in due course we shall return to his own words upon the subject.

Since his time many papers have been written about it, short, long and in many languages. Nylén's clinical and animal studies are well known, in particular his monograph on positional nystagmus occurring in intracranial tumours [16], and in a recent survey of the subject [17] he gives a bibliography of no less than 297 papers written by 192 authors.

Considerable difficulties have been encountered in the preparation of the present communication; difficulties which arise in the main from certain serious deficiencies in the terminology of the subject which now pervades its extensive and confusing literature. Thus, it now seems to be generally agreed that a certain type of positional nystagmus which Nylén defined as the "position changing" type is associated with posterior fossa lesions. This type of positional nystagmus is characterized by the fact that its direction changes when the position of the head is reversed, and it is proposed to exclude it from the present communication. But Nylén also defined another type of positional nystagmus as the "direction fixed" type. In this, certain positions of the head produce nystagmus, and its direction does not change with changes in the position of the head.

Now this, in some respects, corresponds more closely both with what Bárány observed in his case of otolith disease, and with what we have observed in the group of cases now to be described.

It is found, however, on proceeding to this task, that the characteristics of the nystagmus in this, as indeed in any variety of positional nystagmus, cannot be adequately specified in terms of its direction fixation. Furthermore, such a classification takes no note at all of certain other features of the nystagmus which were mentioned very clearly by Bárány and are obviously of great importance; so much so that they must inevitably be taken as our starting point. They are as follows: Firstly,

the character of the nystagmus which is essentially paroxysmal; secondly, the course of the disease which is essentially benign. It is seldom, if ever, we find, associated with any evidence of intracranial disease, and tends to recover with time and simple sedative measures. As will be seen, our evidence goes to show that it is due, as Bárány believed of his case, to a non-progressive lesion of the otolith apparatus. Bárány's own words upon his case may now be quoted. The patient was a 27-year-old woman who had had attacks of vertigo for fourteen days. Hearing was normal, the caloric reactions normal, and the central nervous system normal. Bárány writes:

"My assistant, Dr. Carlefors, first noticed that the attacks only appeared when she lay on her right side. When she did this, there appeared a strong rotatory nystagmus to the right. The attack lasted about 30 seconds and was accompanied by violent vertigo and nausea. If, immediately after the cessation of the symptoms, the head was again turned to the right, no attack occurred, and in order to evoke a new attack in this way, the patient had to lie for some time on her back or on the left side."

Bárány goes on to say that similar observations have been made by himself and others, and the reaction had been attributed to lesions of the semicircular canals. In this case, however, Bárány carried out certain further observations, and demonstrated that the factor precipitating the vertigo was not head movement but head position in space, and for this reason he attributed the condition to a disorder of the otoliths.

Our approach to the study of this condition, of which we have now seen a large number of cases, has been primarily clinical. First comes the matter of symptomatology and in few conditions is careful history-taking of such decisive importance. Apart from the patient's account of his symptoms other points of interest are sex and age incidence, relationship of the symptoms to head injury, to focal infection and to collateral evidence of aural or neurological disease. Finally, note is taken of the duration of the symptoms and their response to treatment.

An otological examination is then carried out with full functional tests of hearing and equilibrium, and lastly an examination is made for positional nystagmus.

Symptoms.—The story given by the patient is characteristically that the giddiness comes on when he lies down in bed or when he turns over in bed, or when such a position is taken up during the day; for instance, in lying down beneath a car or in throwing the head backward to paint a ceiling. The patient sometimes, although not always, recognizes that the onset of the vertigo is associated with this critical position and will say that he does his best to avoid it. He may sometimes also say that he has noticed the phenomenon of adaptation which Bárány described so well in his patients, and can cause his vertigo to disappear by maintaining his head in the disagreeable position, or by taking up this position slowly. The vertigo is essentially transient and it is generally accompanied, but not always, by nausea and, it may be, by vomiting. Cochlear symptoms are generally absent; one other symptom of interest is of discomfort, and it may be of tenderness in the occipital region. Examination of the ears, nose and throat reveals in many cases normal findings, and the same can be said of the usual tests of cochlear and vestibular function. These will be considered after first describing the positional nystagmus and our technique for eliciting it.

The reaction is induced, as Bárány said, by a critical position of the head in space. This can be defined as follows: The patient is laid supine upon a couch with his head just over its end. The head is then lowered some 30 degrees below the level of the couch and turned some 30 degrees to 45 degrees to one side. In taking up this position, the patient is first seated upon the couch with the head turned to one side and the gaze fixed upon the examiner's forehead. The examiner then grasps the patient's head firmly between his hands and briskly pushes the patient back into the critical position. The reaction which results calls for some detailed description.

First of all there is nearly always a marked latent period. Sometimes this is as long as 5/6 seconds. Occasionally it is very short and indeed the reaction may seem to come on at once. This, however, is uncommon. The onset of the nystagmus is nearly always preceded by an appearance of distress. The colour may change; the patients may close their eyes, cry out in alarm and make active efforts to sit up again. At this point it is necessary to reassure the patient and maintain the position of the head. The nystagmus is chiefly rotatory, the direction of the rotation being towards the undermost ear. (*Note.*—In specifying the direction of the rotation reference is made to the displacement of the 12 o'clock point of the corneal circumference.) In addition to the rotatory element there is generally a horizontal component which is again directed towards the undermost ear. The nystagmus increases in a rapid crescendo in a period which may be as short as 2/3 seconds, or as long as 10 seconds. Thereafter it rapidly declines and the patient's distress is relieved. If the patient is then allowed to sit up, a recurrence of the vertigo in a slighter form is generally noted, and if the eyes are examined at this point nystagmus can be seen, the direction of which is, on the whole, reversed. If this is allowed to disappear and the critical supine position is again assumed, the nystagmus again makes its appearance but generally in slighter form and disappears more rapidly than before. After two or three repetitions of this test it is generally found that the reaction has been eliminated altogether and cannot be elicited except, as Bárány pointed out, after a period of rest.

A more detailed consideration will now be given to the oto-rhino-laryngological findings, and the

tests of cochlear and vestibular function. A substantial body of our patients, more than a third, have been found to have entirely healthy ears, noses and throats. Tests of cochlear function have been normal; tests of vestibular function, Romberg, gait and caloric responses have also been normal. Rather more than half of the subjects have exhibited substantial evidence of ear disease. This evidence has generally taken the form of tympanic changes indicative of old and sometimes active catarrhal or suppurative otitis media. In a few cases a severe high-tone deafness has been present alone; in some, due to trauma, in others of obscure ætiology. In most of these, substantial abnormalities of cochlear function, or of the caloric test results were present. In a good many of these cases with ear disease, one ear alone was affected and, as will later be seen, it has been possible to apply this finding to a solution of the problem of localization of the lesion. On the whole, however, it is true to say that evidence of ear disease, although present in some cases, is inconspicuous in the majority and entirely absent in over a third.

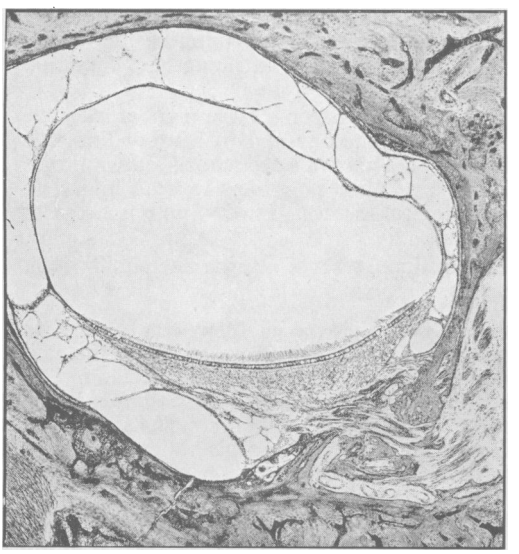

FIG. 8.—(× 15.)

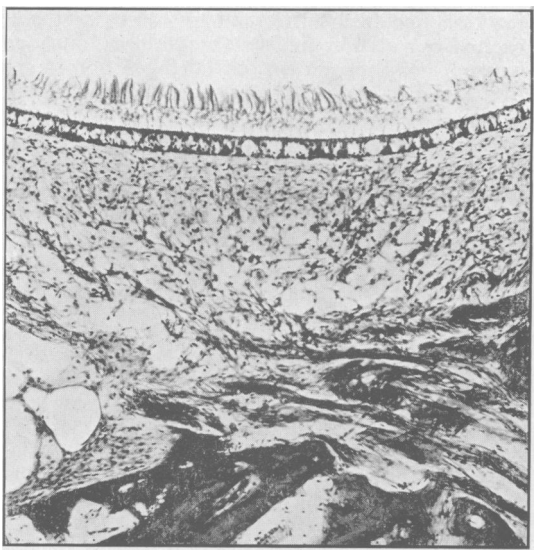

FIG. 9.—(×94.)

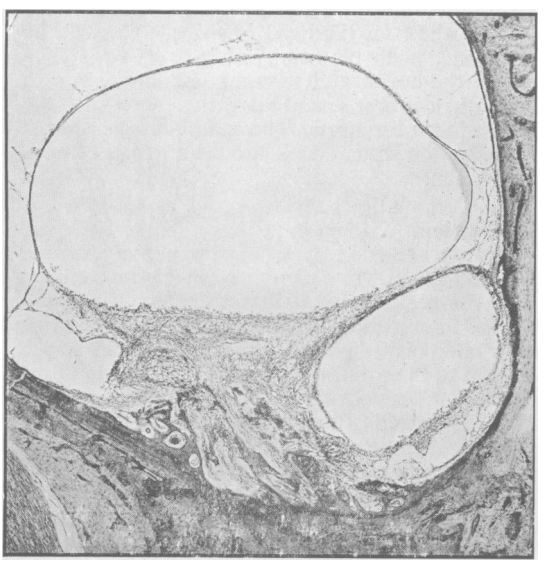

FIG. 10.—(× 15.)

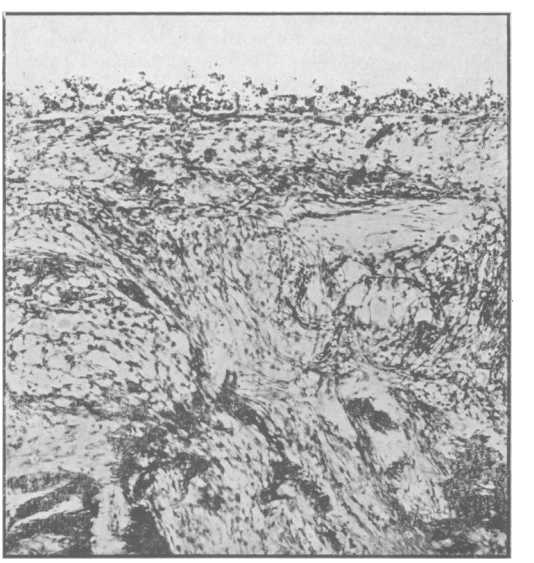

FIG. 11.—(× 94.)

For description of Figs. 8—11 *see* p. 353.

We come, finally, to the course of the disease and the association of the nystagmus with other evidence of neurological disorder. In a good many subjects pain in the neck and occipital region is complained of, and radiological examination has generally revealed some evidence of cervical arthritis. The region, however, affected is chiefly that of the fifth and sixth cervical vertebræ, a very common site in subjects of our predominant age groups, and it has therefore been impossible to attribute any significance thereto. All of our cases have been investigated by our neurological colleagues and, with one or two exceptions of doubtful significance, no evidence has been found of any neurological lesion. The course of the disease is essentially benign. Many of our cases have been followed up for five years or more and in nearly all the symptoms have subsided with sedatives. In a few, infective lesions have been present of the antra or teeth, and these have been eliminated by appropriate surgical measures. It appears likely that the incidence of such infective lesions in our cases has been abnormally high; certainly more so than in cases of Ménière's disease. The evidence for this is, however, inconclusive and it is certainly true to say that in many cases no evidence of infection has been found.

In reviewing the clinical data so far presented it can be said of this disorder that a great deal is now known of its symptomatology and natural history. Much is also known of its physical signs. It is of interest, therefore, to review this knowledge and consider the information which it yields upon the nature of its pathology.

Two things are quite clear. Firstly, the pathological process, wherever or whatever it is, is essentially a benign or self-limiting one. Secondly, the lesion, whatever its nature, is entirely limited to the vestibular apparatus, and here the term "vestibular" is used in its widest sense, to include the labyrinth, vestibular nerve and its central connexions. The questions, therefore, that remain are these: Where exactly is the lesion? and what is its nature?

These we have endeavoured to answer by means of further clinical studies, and by the histological examination of the labyrinth in a human subject.

The clinical evidence will be considered first. The benign character of the disorder and the fact that its manifestations are entirely vestibular exclude at once the possibility that it is due to any destructive lesion, vascular, neoplastic, inflammatory or degenerative within the brain-stem or VIII nerve. If it were, then the occasional occurrence of involvement of other nervous pathways within the brain-stem which lie close to the vestibular neurones would be inevitable. Furthermore, some evidence of the destruction of the vestibular neurones themselves would be apparent, as, for instance, changes in the caloric test results which are so characteristic of vestibular neuronitis and which we have attributed to a toxic destruction of the vestibular neurones within the brain-stem.

It is conceivable, of course, that the nystagmus might be due to some temporary vascular disorder of the brain-stem dependent upon some vascular abnormality. Here it is well known that De Kleyn [18] suggested this very possibility and brought forward good anatomical evidence that in some cases at least an abnormality of one vertebral artery rendered it susceptible to occlusion by certain head positions of the very kind that we employ for eliciting the typical reaction of positional nystagmus. We have been in the habit, from time to time, of examining typical cases without any neck-twisting, and recently we have adopted even more elaborate precautions to exclude this possible source of artefact, if such it could be called.

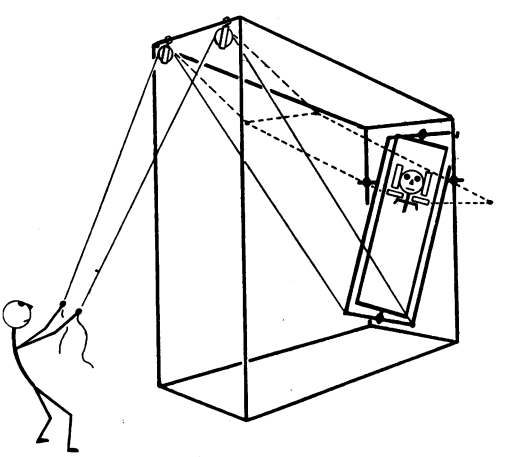

FIG. 7.

By means of apparatus shown in Fig. 7 it is possible to move the patient *en masse* into the critical position, and under these conditions the characteristic nystagmic reaction has been found to make its appearance as usual. It still remains conceivable that some kind of reversible lesion of the central vestibular neurones due

to infection or injury, with or without some anatomical aberration, might bring about the typical reaction to posture now described. Nevertheless, the very fact that the condition *never* exhibits evidence of any extra-vestibular involvement, together with the absence of any evidence of destruction of vestibular neurones, as for instance changes in the caloric responses, makes the possibility of a central lesion exceedingly remote, and on this purely clinical evidence alone we have been inclined to localize the lesion more peripherally, and further, to believe that it has an essentially irritative basis.

Two questions of great interest now arise: Is the lesion in the labyrinth at all? If so, which is the affected labyrinth? And here it has been possible to advance our ideas very considerably by the further analysis of the clinical evidence.

The total number of our cases is 100. Age and sex incidence are given in Table V. The cases have also been divided into three groups in a manner designed to establish the role, nature and localization of ear disease as a possible cause of the positional nystagmus.

The analysis is presented in Table VI.

TABLE V.—POSITIONAL NYSTAGMUS OF THE BENIGN PAROXYSMAL TYPE. 100 CASES

Age Distribution

Age (years)	20–29	30–39	40–49	50–59	60–69	Over 70	Total
Number ..	4	18	27	33	13	5	100

Sex Distribution

Male	52	Total	100
Female	48		

TABLE VI.—POSITIONAL NYSTAGMUS OF THE BENIGN PAROXYSMAL TYPE

The Role of Ear Disease as a Causative Factor

	Number of cases
Group I:	
No evidence of ear disease	34
Group II:	
Slight evidence of ear disease (abnormality of caloric responses only) ..	11
Group III:	
Substantial evidence of ear disease (gross middle ear infections, labyrinthine trauma, &c.)	55
Total	100

In the first of these three groups there are 34 cases with no evidence whatsoever of disease of either ear; this group, therefore, provides no evidence of localization. In the next group of 11 cases slight evidence of ear disease was present, and in the majority of these the disease was unilateral. In the third group of 55 cases the evidence of ear disease was more obvious and again, in a large proportion of cases, the disease was unilateral. Correlation of this evidence of ear disease in these two last groups of cases with the direction of the nystagmus, leads to two important conclusions:

(1) That ear disease does play an important role in the causation of the nystagmus.

(2) That the side of the ear disease is related to the direction of the nystagmus in a systematic manner.

Going back to

Group I: In 31 of these 34 cases the positional nystagmus was unilateral, directed towards the undermost ear. In the other 3 cases, the positional nystagmus was bilateral and again directed towards the undermost ear. It is proper to say of these 34 cases that no evidence is provided as to the localization of the lesion responsible for the nystagmus. Further, that the lesion, if it is in one or other labyrinth, has caused no other demonstrable disturbance of its function.

Group II: In all 11 cases the only evidence of ear disease was an abnormality of the caloric test responses. In 4 of these the caloric abnormality was bilateral. In all 4 the positional nystagmus was unilateral and directed towards the undermost ear. In all of the other 7 cases, in which the abnormality was unilateral, the positional nystagmus was also unilateral and directed towards the side of the caloric abnormality when this was undermost. It is necessary to comment on the fact that in all of the 7 of these 11 cases in which an aural lesion was present, even in the form of a caloric abnormality, the positional nystagmus was always directed towards the affected side when this was undermost. This strongly suggests that the lesion responsible for the positional nystagmus was located within the undermost ear.

We come finally to

Group III: The cases in Group III consist of 55 subjects with substantial evidence of ear disease. This evidence is analysed in Table VII.

TABLE VII:—POSITIONAL NYSTAGMUS OF THE BENIGN PAROXYSMAL TYPE

Group III: 55 cases with substantial evidence of ear disease	Bilateral	Unilateral	Direction of positional nystagmus: Towards affected ear when undermost	Towards affected ear when uppermost
A. Evidence of otitis media (suppurative or severe catarrhal)	11	15	15	0
B. Evidence of neuro-labyrinthitis (mumps or syphilis)	1	2	0	2
C. Evidence of inner ear trauma	12	6	5	1
D. Other evidence of ear disease (nerve deafness of obscure ætiology)	7	1	1	0
	31	24	21	3

The 31 cases in which the disease was bilateral can be put aside as presenting no evidence of localization. 24 cases are left in which the ear disease was unilateral. It will be seen that in no less than 21 of these the direction of positional nystagmus was towards the diseased ear when this was undermost. This evidence demonstrates again that ear disease is an important factor in causing the nystagmus. Furthermore, that the nystagmus is directed towards the side of the lesion when this is undermost.

We are thus directed to the conclusion that the lesion *is* a peripheral one and in the labyrinth towards which, when undermost, the nystagmus is directed. Consideration may next be given to the nature of the lesion, and here again clinical studies have proved of decisive importance. The benign course of the disorder makes a neoplastic lesion impossible. The usual absence of cochlear dysfunction and the entirely different character of the vertigo differentiates it completely from the typical hydrops of Ménière's disease, and the remaining possibility is thus of a chronic lesion due to infection, trauma or vascular disease. The lesion certainly affects the otoliths and, since it is so often associated with normal caloric responses, it follows that it is more likely to be irritative in character than destructive.

This concludes our clinical evidence bearing upon the nature and localization of the lesion responsible for positional nystagmus of the benign paroxysmal type.

We have been able to derive supporting evidence from the histological examination of the labyrinths of a characteristic case and an account of our findings is appended.

The case was that of a woman aged 40, a patient of Sir Charles Symonds', who died at the National Hospital, Queen Square, on December 3, 1947. For twenty years she had suffered from vertigo with deafness of unknown cause of the right ear. Her terminal illness and death were due to a glioma affecting the basal ganglia and the upper part of the brain-stem on the left-hand side. On examination a few months before death there was a severe deafness of the right ear of the inner ear type without evidence of tympanic disease. The caloric responses were brisk and normal on both sides and a positional nystagmus of the benign paroxysmal type was present to the right with the right ear undermost. Her symptoms under these conditions reproduced the vertigo from which she had suffered for twenty years. On histological examination the left labyrinth was normal. The right labyrinth showed a severe degeneration of the spiral ganglion in the cochlea which was the essential cause of the deafness. The ampullæ of the semicircular canals appeared normal. In the maculæ of the utricle and saccule, however, very unusual changes were present, in particular the utricle.

In Fig. 8 is shown, for comparison, the appearance of the normal, healthy human utricular macula. The layer of sensory cells is seen evenly arranged with the superimposed otolith membrane. Beneath the layer of sensory cells lies a loose connective tissue meshwork, in which run the fibres of the utricular nerve.

In Fig. 9 is shown a view at higher magnification of the sensory epithelium and the underlying connective tissue meshwork.

In Fig. 10 is shown a view of the macula of the utricle in our case of positional nystagmus. The outstanding feature is the absence of the otolith membrane, the disorganization of the sensory epithelium and certain gross tissue changes in the connective tissue meshwork underlying the epithelium. Its depth is greatly increased. A certain amount of new bone formation has taken place, and at certain points a considerable cellular infiltration is present. This is better seen at higher magnification in Fig. 11.

In Fig. 11 it can be seen that in addition to the absence of the otolith membrane and the disorganization of the sensory cells, there is also present a considerable thickening of the sub-epithelial connective tissue network with the presence here and there of irregular cellular infiltrations. At one point there occur a number of irregular spaces occupied by fluid or cell remnants. The general picture is one of chronic tissue changes resulting either from infection or trauma and it accords very well with our conception of the responsible lesion which we have reconstructed from our clinical evidence. Changes very similar in character but lesser in degree were present in the macula of the saccule.

This concludes our clinical and pathological evidence on the subject of this variety of positional nystagmus. As already stated, it would seem essential to describe it as the benign paroxysmal type

on account of certain outstanding clinical features which distinguish it just as much as its directional characteristics.

In order to achieve clarity emphasis has been laid in the course of this communication upon such facts—on the whole many and weighty—which fortify the central theme of our argument. Certain discrepancies exist; they have not been overlooked and will be given attention in the course of further studies. We do not think that they will be found to invalidate our main conclusion which is that positional nystagmus of the benign paroxysmal type, first described by Bárány in 1921, is due, as Bárány believed, to otolith disease. The lesion consists of chronic tissue changes which may be due to trauma, chronic infection or possibly to vascular disease. It affects, and may be confined to, the sensory epithelium and the sub-epithelial connective tissue of the utricle and saccule of the labyrinth towards which, when undermost, the positional nystagmus is directed.

ACKNOWLEDGMENTS

It is a pleasure to acknowledge the great help that we have received in the course of these investigations from our colleagues, the physicians and surgeons of the National Hospital, Queen Square, who have so kindly put their cases at our disposal; in particular, to Sir Charles Symonds, 2 of whose cases have proved of special importance; also to Dr. C. H. Edwards, who gave us considerable help in the early stages of the preparation and analysis of the clinical findings of our cases of positional nystagmus. Finally, for the construction of the apparatus shown in Fig. 7 and of other special test equipment, and for the preparation and photography of the histological material we are greatly indebted to the laboratory staff of the Otological Research Unit of the Medical Research Council.

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Sir Charles Symonds' paper on "The Significance of Vertigo in Neurological Diagnosis" will appear in the *Journal of Laryngology and Otology.*

[*February* 1, 1952]

The papers by Mr. F. C. W. Capps and Mr. Munro Black on "Glomus Jugulare Tumours" will be published in the *Journal of Laryngology and Otology.*

A paper on "Eosinophil granuloma" read by Mr. A. R. Dingley will also be published in that Journal.